

CLAIMS

1. A method for preparing cross-linked polyelectrolyte multilayers films, wherein said method comprises the reaction of complementary functional groups : carboxylic groups
5 and amino groups, present in the polymers that constitute the multilayer film, in the presence of a coupling agent, as to form amide bonds.
2. A method according to claim 1, wherein the used polyelectrolyte multilayers are assembled via any complementary interaction, especially electrostatic attraction and
10 hydrogen bridging.
3. A method according to one of the preceding claims, wherein the polyelectrolyte multilayers films are biocompatible.
- 15 4. A method according to one of the preceding claims, wherein said polyelectrolyte multilayers comprise at least one layer pair of cationic polyelectrolytes and anionic polyelectrolytes.
- 20 5. A method according to one of the preceding claims, wherein said polyelectrolyte multilayers comprise at least one layer pair of cationic polyelectrolytes and anionic polyelectrolytes and the number of said layer pairs is from 1 to 1000, preferably from 2 to 100, more preferably from 5 to 60.
- 25 6. A method according to one of the preceding claims, wherein said carboxylic groups and amino groups are attached by covalent bonds to polyelectrolytes.
7. A method according to one of the preceding claims, wherein the polymers that constitute the multilayer film comprise cationic polyelectrolytes which present free amino groups and anionic polyelectrolytes which present free carboxylic groups.
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8. A method according to one of the preceding claims, wherein the polymers that constitute the multilayer film comprising anionic polyelectrolytes which present free carboxylic groups are selected in the group consisting of polyacrylic acid,

polymethacrylic acid, acid, poly(D,L-glutamic) acid, polyuronic acid (alginic, galacturonic, glucuronic...), glycosaminoglycans (hyaluronic acid, dermatan sulphate, chondroitin sulphate, heparin, heparan sulphate, and keratan sulphate), poly(D,L-aspartic acid), any combination of the polyamino acids, and mixtures thereof.

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9. A method according to one of the preceding claims, wherein the polymers that constitute the multilayer film comprising cationic polyelectrolytes which present free amino groups are selected in the group consisting of poly(D,L-lysine), poly(diallyldimethylammonium chloride), poly(allylamine), poly(ethylene)imine, 10 chitosan, Poly(L-arginine), Poly(ornithine), Poly(D,L-hystidine), poly(mannoseamine, and other sugars) and more generally any combination of the polyamino acids and mixtures thereof.

10. A method according to one of the preceding claims, wherein the polyelectrolyte 15 multilayers can further comprise polymers with different functional groups, including cationic (sulfonium, phosphonium, ammonium, hydroxylamine, hydrazide), anionic (including poly(styrene sulfonate), poly(phosphate), polynucleic acid...) and neutral (including polyacrylamide, polyethylene oxyde, polyvinyl alcohol) polymers.

20 11. A method according to one of the preceding claims, wherein the polyelectrolyte multilayers comprise a variety of materials, preferably synthetic polyions (polymers presenting ions), biopolymers such as DNA, RNA, collagen, peptides (such as a RGD sequence, Melanoma stimulating Hormone, or buforin), proteins, and enzymes, cells, viruses, dendrimers, colloids, inorganic and organic particles, dyes, vesicles, nano(or 25 micro)capsules, nano(or micro)particles, polyelectrolytes complexes, free or complexed drugs, cyclodextrins, and mixtures thereof.

12. A method according to one of the preceding claims, wherein the coupling agent is a carbodiimide compound.

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13. A method according to one of the preceding claims, wherein the coupling agent is a compound of formula (I) :



wherein R and R', which are identical or different, represent an alkyl or aryl group, preferentially an C1-C8 alkyl group.

14. A method according to claim 13, wherein the coupling agent is 1-ethyl-3-(3-
5 dimethylaminopropyl) carbodiimide (EDC).

15. A method according to one of the claims 1-11, wherein the coupling agent is a peptide-coupling agent.

10 16. A method according to one of the preceding claims, wherein the reaction of carboxylic groups and amino groups of the polyelectrolyte multilayers in the presence of a coupling agent is carried out also in the presence of N-hydroxysuccinimide compounds.

15 17. A method according to claim 16, wherein the reaction of carboxylic groups and amino groups of the polyelectrolyte multilayers in the presence of a coupling agent is carried out also in the presence of N-hydroxysulfo succinimide para-nitrophenol, or dimethylaminopyridine.

20 18. A method of coating a surface, comprising (1) sequentially depositing on a surface alternating layers of polyelectrolytes to provide a coated surface presenting complementary reactive groups: amino and carboxylic groups, wherein a first (or conversely second) polymer is a cationic polyelectrolyte and a second (or conversely first) polymer is an anionic polyelectrolyte, and (2) reacting said complementary reactive groups of the coated surface in the presence of a coupling agent, as to form amide bonds
25 between said complementary reactive groups.

19. A method according to claim 18, comprising (1) sequentially bringing a surface into contact with polyelectrolyte solutions thereby adsorbing alternated layers of polyelectrolytes to provide a coated surface presenting amino and carboxylic groups,
30 wherein a first (or conversely second) polymer is a cationic polyelectrolyte and a second (or conversely first) polymer is an anionic polyelectrolyte, and (2) reacting amino and carboxylic groups of the coated obtained surface in the presence of a coupling agent, as to form amide bonds.

20. A method according to claim 18 or 19, wherein depositing on a surface alternating layers of polyelectrolytes includes dipping, dip-coating, rinsing, dip-rinsing, spraying, inkjet printing, stamping, printing and microcontact printing, wiping, doctor blading or
5 spin coating.
21. A method according to one of the preceding claims 18-20, wherein the depositing process involves coating and rinsing steps.
- 10 22. A method according to one of claims 18-21, wherein the carboxylic groups and amino groups are attached by covalent bonds to polyelectrolytes.
23. A method according to one of claims 18-22, wherein anionic polyelectrolytes which present free carboxylic groups are selected in the group consisting of polyacrylic acid,
15 polymethacrylic acid, acid, poly(D,L-glutamic) acid, polyuronic acid (alginic, galacturonic, glucuronic...), glycosaminoglycans (hyaluronic acid dermatan sulphate, chondroitin sulphate, heparin, heparan sulphate, and keratan sulphate), poly(D,L-aspartic acid), any combination of the polyamino acids, and mixtures thereof.
- 20 24. A method according to one of claims 18-23, wherein cationic polyelectrolytes which present free amino groups are selected in the group consisting of poly(D,L-lysine), poly(diallyldimethylammonium chloride), poly(allylamine), poly(ethylene)imine, chitosan, Poly(L-arginine), Poly(ornithine), Poly(D,L-hystidine), poly(mannoseamine, and other sugars) and more generally any combination of the polyamino acids and
25 mixtures thereof.
25. A method according to one of claims 18-24, wherein polyelectrolyte multilayers can further comprise polymers with different functional groups, including cationic (sulfonium, phosphonium, ammonium, hydroxylamine, hydrazide), anionic (including
30 poly(styrene sulfonate), poly(phosphate), polynucleic acid...) and neutral (including polyacrylamide, polyethylene oxyde, polyvinyl alcohol) polymers.

26. A method according to one of claims 18-25, wherein the coupling agent is a carbodiimide compound.

27. A method according to claim 26, wherein the coupling agent is a compound of
5 formula (I) :



wherein R and R', which are identical or different, represent an alkyl or aryl group, preferentially an C1-C8 alkyl group.

10 28. A method according to claim 27, wherein the coupling agent is 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC).

29. A method according to one of claims 18-25, wherein the coupling agent is a peptide coupling agent.

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30. A method according to any one of the claims 18-29, wherein step (2) is carried out also in the presence of N-hydroxysuccinimide compounds.

31. A method according to claim 30, wherein step (2) is carried out also in the presence of
20 N-hydroxysulfo succinimide para-nitrophenol, or dimethylaminopyridine.

32. A method according to any one of claims 18-31, wherein the coated surface of step (1) further comprises a variety of materials, including synthetic polyions (polymers presenting ions), biopolymers such as DNA, RNA, collagen, peptides (such as a RGD
25 sequence, Melanoma stimulating Hormone, or buforin), proteins, and enzymes, cells, viruses, dendrimers, colloids, inorganic or organic particles, dyes, vesicles, nano(micro)capsules and nano(micro)particles, polyelectrolytes complexes, free or complexed drugs, cyclodextrins, and mixtures thereof.

30 33. An article coated by a method according to any one of the claims 18-32.

34. A coated article according to claim 33, wherein said coated article is biocompatible.

35. A coated article according to claim 33 or 34, wherein said article is selected from the group consisting of blood vessel stents, angioplasty balloons, vascular graft tubing, prosthetic blood vessels, vascular shunts, heart valves, artificial heart components, pacemakers, pacemaker electrodes, pacemaker leads, ventricular assist devices, contact lenses, intraocular lenses, sponges for tissue engineering, foams for tissue engineering, matrices for tissue engineering, scaffolds for tissue engineering, biomedical membranes, dialysis membranes, cell-encapsulating membranes, drug delivery reservoirs, drug delivery matrices, drug delivery pumps, catheters, tubing, cosmetic surgery prostheses, orthopedic prostheses, dental prostheses, bone and dental implant, wound dressings, sutures, soft tissue repair meshes, percutaneous devices, diagnostic biosensors, cellular arrays, cellular networks, microfluidic devices, and protein arrays.

36. A coated article according to any one of the claims 33-35, wherein said coated article further comprises a variety of materials, including synthetic polyions, biopolymers such as DNA, RNA, collagen, peptides (such as a RGD sequence, Melanoma stimulating Hormone, or buforin), proteins, and enzymes, cells, viruses, dendrimers, colloids, inorganic and organic particles, vesicles, nano(micro)capsules and nano(micro)particles, dyes, vesicles, nano(micro)capsules and nano(micro)particles, polyelectrolytes complexes, free or complexed drugs, cyclodextrins, and mixtures thereof.